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INFLUENZA: PAST AND PRESENT

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INFLUENZA: PAST AND PRESENT

By

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Lafayette College, A.B. 1955

A thesis presented to the
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Chapter I

Historical

Mention has been made of what we now term influenza epidemics by most every ancient writer sometime during the course of his literary career. Hippocrates and Livy both wrote of the curious, sweeping illness of 412 B.C..¹ Diodorus Siculus described an influenza-like epidemic which swept through the Athenian army in Sicily in 415 B.C.. Warren Vaughan, in his monograph on influenza, felt that the pestilence which took the lives of thousands of Greek soldiers during the siege of Syracuse was in retrospect influenza. He goes on to mention reports in 876 A.D. of a cough which swept through Italy taking the lives of many of Charlemagne's troops.² Dr. August Hirsch, German physician and medical historian of the nineteenth century believed the first epidemic that can be definitely said to be influenza occurred in 1173. This had been misinterpreted by some to mean that the first influenza epidemic took place in 1173, but a more accurate translation from the German has clarified the issue.

An influenza-like disease designated Furacht or Slaodan was described in an Irish manuscript in the fourteenth century as resembling the devil's prostration, and was mentioned again in the fifteenth century in The Annals of the Four Masters as epidemic throughout Ireland.³ Gaelic documents at that time used the word creaton from creat, meaning chest, to imply influenza.

¹ Vaughan, Victor C. Epidemiology and public health. St. Louis, Mo., C. V. Mosby Company, 1922, vol. 1, p. 300.

² Vaughan, Warren T. Influenza. An epidemiologic study. Amer. J. Hyg., 1921, monograph series no. 1, p. 2.

³ Thompson, E. Symes. Influenza or epidemic catarrhal fever. London, Percival and Company, 1890, p. 1.

The first accurate and complete description of an influenza epidemic in the English-speaking world came to us in 1749 from the pen of Dr. Thomas Short of London.¹ Dr. Short endeavored to describe the course of an influenza epidemic which struck London in 1510. He postulated that the disease began in Africa, crossed the Mediterranean Sea in 1509 to Sicily, proceeded through Italy, passed over the Alps into Germany approximately two months later, struck throughout western Europe scarcely missing a family, and finally crossed the Channel into England in the spring of 1510. Dr. Short went on to describe the symptomatology quite accurately, noting headache, difficulty in breathing, hoarseness, anorexia, weakness, a productive cough, and severe prostration of varying degrees in almost every case. He went on to say that the disease in 1510 had a duration of approximately eight days, and claimed only the lives of children. The physicians of the day were unanimous in their therapy using bole ammonias, oily lintus, and pectoral troches. The use of blood-letting, a popular medical treatment of the times, was found to be contraindicated, and when used, promoted serious complications and often death. Dr. Short, after his initial work, went on to describe similar periods of sickness which swept across England in 1557, 1580, and again in 1610. He ventured in his later works to postulate the positive association of the epidemics with natural phenomena such as earthquakes, volcanic eruptions, and celestial displays. Short's writings were instrumental in establishing a precedent in description which later investigators such as Willis, Sydenham, and Huxam followed and elaborated upon.

Willis, in his Practice of physick, 1685, recognized and recorded

¹ Thompson, E. Symes. Op. cit., p. 4.

the uniformity of symptomatology and course in the English epidemic of 1658, and remarked on the similarity to Short's findings 150 years earlier.¹ Dr. Willis was greatly interested and concerned in Short's postulation that influenza bore a close relationship to concurrent physical and geological upheavals. In 1658 Willis took issue with Short's thesis, and stated that he could find no relationship between the occurrence of influenza and physical phenomena, temperature changes, or geological happenings. His records served as an example to other workers in medical observation, and in fifty-five of the years between 1800 and 1875 epidemic influenza was reported by a medical observer somewhere in the world. Abbott, writing about the 1889-90 epidemic, states that in the fourteenth century there were six influenza epidemics, seven in the fifteenth, eleven in the sixteenth, sixteen in the seventeenth, and eighteen in the eighteenth century.²

From these reports we see that man's investigative mind enabled him to recognize long before he recorded the existence of a curious disease which struck entire populations as it swept from one locale to another. He referred to this specific malady as Gallant's disease, Pfeiffer's malaise, and catarrhal fever to mention only a few which have remained until today; however, it was the Florentines who first used the word influenza to designate the disease as we now know it.³

The misery of an epidemic and the realization that there were more epidemics to come plagued medical science throughout the nineteenth century. A cause and effect relationship was sought, but continued to evade medical researchers time and time again. In the midst of the 1892 epidemic,

¹ Francis, Thomas Jr. Influenza: the new acquaintance. Ann. int. med., 1953, 39, 204.

² Vaughan, Victor C. Op. cit., vol. 1, p. 300.

³ Wyeth Laboratories. Influenza 1957, 1957, 21.

R. Pfeiffer isolated the bacillus now called hemophilus influenza, and postulated this to be the cause for the epidemic disease.¹ This observation gained wide acceptance, and Pfeiffer's bacillus was held responsible for the influenza epidemic of 1899. Medicine now believed it had found the long evasive etiological agent, and cure and control were just around the corner. Much evidence poured in during the next decade to substantiate and support Pfeiffer's findings. The world now felt better prepared than ever before for influenza to strike again. Pfeiffer, his associates, and most epidemiologists of the time waited patiently. Their wait was short, for in January 1918 an outbreak of what seemed characteristic of influenza appeared in northern China. The primary, localized outbreak was recognized, but was not considered widespread enough to be of much consequence. Little did investigators realize that within a year and a half, twenty million people would die as a direct result of this seemingly insignificant, localized, Chinese outbreak.

¹ Smith, David T., Conant, Norman F. et al. Zinsser bacteriology. New York, Appleton-Century-Crofts, Inc., 1957, p. 732.

Chapter II

The 1918 Epidemic

The first report of influenza in the United States came from an army post, Camp Funsten, on March 5, 1918. By the end of March a mild form of the disease was being reported from almost every city east of the Mississippi. There were many current opinions at this time concerning the place of the primary focus of the disease. Clifford Gill believed that the continental land masses of central Asia and Canada, because of their favorable climatic conditions, served as endemic homes for potential epidemics and remained reservoirs of infection. He went on to apply his quantum theory to the epidemic which explained the outbreak in terms of a loss of equilibrium between infection and immunity.¹ Chaufford, Netter, and MacNeal believed the pandemic had its origin in France, Alberto Lutraria placed the focus in the United States, and McNalty stated his not hitherto mentioned belief that the pandemic had an origin consisting of multiple foci. While these various views were being debated, influenza made its first appearance among American troops in Brest, France, in April, 1918.² Many thought that this event was the start of the soon present European epidemic, but later reports showed that there were reports of mild, documented cases in England before the arrival of the American troops in France. Regardless of the focus or foci, the epidemic reached Scotland, Spain, Greece, and Egypt by May, and engulfed all Europe, China, and India by July 1918. As ships returned American troops to Boston in August, the mild cases aboard ship provided the spark which was respon-

¹ Gill, Clifford A. The genesis of epidemics and the natural history of disease. London, Bailliere, Tindall, and Cox, 1926, p. 223.

² Burnet, F. M. and Clark, Ellen. Influenza. Melbourne, Australia, Macmillan and Co. Ltd., 1942, p. 70.

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sible for the 1918 epidemic as we now remember it. By October 5th, 1,214 people had died in Boston, and the whole Atlantic seaboard now experienced an epidemic which was going to prove fatal to 390 out of every 100,000 people in the United States.¹ Within six weeks the entire country had been attacked. With the exception of San Francisco, the eastern seaboard cities reported the highest mortality rates. Philadelphia experienced the highest rate in the country, losing .77 per cent of its population.² Victor C. Vaughn, at this time, classically defined influenza clinically as an acute febrile disease of extreme communicability, characterized by catarrh of the respiratory tract accompanied by pains in the head and musculature.³ The period of incubation usually was from two to four days, with a sudden onset and marked prostration. The duration varied from a few days to several weeks depending upon the severity of the attack.

The explosive outbreak in the fall of 1918 was characterized by many unexpected occurrences. Public health reports in 1920 state that the incidence was highest among the 5 to 9 and 23 to 34 year-old groups.⁴ Incidence was 6 per cent higher in the male population, and whites were more commonly infected than negroes. It was also shown that the attack rate increased as the number of rooms per house decreased. Mortality

¹ Burnet, F. M. and Clark, Ellen. Op. cit., p. 70.

² Vaughan, Victor C. and Palmer, George T. Communicable disease in the United States Army during the summer and autumn of 1918. J. Lab. Clin. Med., 1919, 4, 594.

³ Vaughan, Victor C. Op. cit., vol. 1, p. 297.

⁴ Frost, W. H. Influenza - prevalence in the United States. Pub. Hlth. Rep. (Wash.), 1920, 35, 579-598.

statistics showed that the highest death rates were found among both males and females under five years of age, males between twenty and forty years, and both males and females over sixty. By the fall of 1918 nearly four million men were interned in the United States military service. During the four autumn months of 1918, 338,343 cases of influenza were reported to the Surgeon General.¹ This constituted one out of every four new recruits. Of these, one out of every 67 died as a result of influenza or related pneumonia.

Given no chance to breath a sigh or regroup its forces after the first explosive wave in the fall, the country was engulfed in a series of recrudescences. These generally proved to be somewhat milder than the autumn wave, with an exception seen in certain cities which suffered to a greater extent than during the first wave. Pearl found, in his study consisting of 40 cities, that 65 per cent showed two peaks of mortality, the second seven weeks after the first, 20 per cent showed three mortality peaks, and 15 per cent showed only one mortality peak.

Thus, in summary, the United States' virst contact with influenza came in the form of a mild episode in the spring of 1918. The severe phase, accompanied by high mortality, arrived that autumn, and a generally mild series of recrudescences followed in early 1919 and again in 1920. All in all, the epidemic clinically affected twenty million people in the United States and was responsible for a half million deaths.²

¹ Vaughan, Victor C. and Palmer, George T. Op. cit., p. 592.

² Wyeth Laboratories. Influenza 1957, 1957, p. 28.

Chapter III

The 1918 Epidemic in Easton, Pennsylvania

As an example of the effect the 1918 influenza epidemic had on the life of a community, I have chosen Easton, Pennsylvania. Being a resident of this community for 25 years made it possible for me to gain ready access to town medical records as well as to those of private physicians who served the community during this epidemic.

Easton is a quiet, medium-sized, town of approximately thirty thousand people, located on the west bank of the Delaware River, separating Pennsylvania from New Jersey. It was founded by Thomas Penn, settled by German settlers, and played an important role in the development of Pennsylvania as a colony and later as a state. In 1776 Easton was the first place in our young country to display a national flag containing stars and stripes. This original flag is now hanging in a place of honor at the Easton Library. In 1832 Lafayette College was founded in Easton, and the town grew culturally, industrially, and agriculturally until it soon became the county seat of Northampton County. Being close to New York and also Philadelphia, Easton in the nineteenth century served as a hub whence the state's coal and steel exports were shipped to both seaport cities. The following report of the influenza epidemic in Easton in the fall of 1918 comes from descriptions found in two Easton newspapers of the time, county Medical reports, and from word of mouth passed on to me by physicians who played active roles in the epidemic.

The headlines of the Easton Express on September 20, 1918 read, "Attack on Yankee Lines Cost Huns Many Men; British At Outposts Of Germany's Strongest Positions." The war in France now occupied the front

page of every American newspaper. By the 4th of July 1918, a quarter of a million American troops were engaging the Germans in the trenches of France. General March announced that already a million of our boys had embarked for France, and movement of the second million was being undertaken. The war was now at the doorstep of every American family. Colleges were closing their doors and forming training corps. Local sports heroes were being followed day by day with their respective companies over there, and the people at home were doing their share by observing meatless Tuesday and heatless Thursday. The Kaiser had not foreseen the ability of this young country to mechanize in such a short time to meet the challenge of the German war machine.

Far at the bottom of the second page of the Express there appeared on September 20th a fill-in article that bore the odd inscription "Spanish Influenza." The article went on to say that one of the Haffey boys of South Easton, home on a furlough from Camp Dix, developed a mild case of what was thought to be Spanish Influenza. Bill told his family that all the boys at camp were sick, but not to worry. Bill returned to camp, none the worse, but soon his two sisters were bed-ridden with the same sort of complaints.

The column was longer and the type bolder by September 25th. Thirty-six deaths, Bill Haffey, among them, were reported at Camp Dix in one day. The total for the week now stood at 96. More men had succumbed than had died in the entire previous history of the camp. Additional army surgeons arrived and were assigned at once to relieve the overworked base hospital staff. From Washington came the announcement that the government would mobilize special medical and nursing units to stamp out influenza in the

camps as well as at home. Provost Marshal General Crowder cancelled the call for entrainment of 142,000 draft registrants between October 7th and 11th when the death rate reach 4.4 per cent of new recruits.

From Lafayette College in Easton came the report of 80 mild flu cases among the military corps. Captain Parker, camp commander, cancelled the annual military ball, highlight of the wartime social season. The students and military personnel gathered on the college quadrangle to demonstrate their vivid disapproval of Captain Parker's decision. The following day 35 more new cases reported to the infirmary.

The Pennsylvania State Board of Health called an emergency meeting September 28th to discuss their plans to fight Spanish Influenza. Dr. E. M. Green of Easton reported that from his personal experience the victims were generally in their teens or early twenties. He said that the disease was unquestionably spread by persons coughing and sneezing. The best thing for a person therapeutically was to take a warm bath, go to bed, and send for the doctor. The type was now bold and the columnn long as Easton seemed to be in the grip of the disease with four deaths reported on September 30th. Hundreds of cases were reported, school children remained at home, stores and factories were operated with only akeleton crews, and Lafayette College was put under quarantine by Captain Parker. Easton Hospital announced that it could only admit emergency and accident patients due to its crowded wards. Congress now appropriated one million dollars to stamp out the disease. An Easton doctor reported that deaths from influenza were definitely associated with secondary pneumonia. Now the people of Easton were beginning to realize that they would have to fight for their lives at home as earnestly as their sons were fighting in France.

the present of the world, and the future of the world, is a matter of the greatest importance to the human race.

The world is a vast and complex system, and it is our duty to understand it and to improve it.

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The first day of October 1918 brought hope to the hearts of American families. They read that Germany was on the verge of internal revolution. Huge crowds were reported staging peace demonstrations in Berlin and demanding the ousting of the military oligarchy. In addition, other good news greeted the Easton area readers. Dr. E. M. Green reported that the flu epidemic had reached its peak in Pennsylvania. He stated that conditions were not as bad as the grip epidemic of 1889 and 1890, and if the weather remained good, the disease would soon disappear. Dr. Green went on to say that the name Spanish Influenza had been given to the epidemic, but doctors agreed that the disease was unquestionably the same as had been known by the names German Influenza, Russian Influenza, and La grippe. It was caused by a micro-organism, and was spread by coughing and sneezing. Five more deaths and a hundred more new cases followed this report. It was now plain the epidemic was far from over. Easton's City Council along with Mayor Nevin decided, after the report of eight more deaths on October 3, to close all theaters, dance halls, and saloons within 48 hours. School authorities were ordered to send home all children who coughed or sneezed, and trolley cars were to have at least three windows open on each car. The following day these regulations were made state wide by the State Department of Health, and were extended to lodge rooms, bowling alleys, pool parlors, and churches. The board of health distributed 1,500 placards throughout the city, illustrating the proper safeguards to prevent the spread of the disease. Thirteen men were arrested in downtown Easton for failing to observe the anti-spitting ordinance. The men spent the night in the city jail. Nine were released the next day, but four remained to receive medical treatment for influenza.

The first and most important step in the process of creating a new business is to identify a market need. This is often done by conducting market research, which involves gathering information about the target market and its needs. Once a market need has been identified, the next step is to develop a business plan. This plan should outline the company's goals, strategies, and financial projections. It should also include a description of the products or services to be offered and the marketing and sales strategies to be used. Once the business plan is complete, the entrepreneur can begin to raise capital and launch the business. The final step in the process is to monitor and evaluate the business's performance. This involves tracking sales, expenses, and other key indicators of success. If the business is not performing well, the entrepreneur may need to make adjustments to the business plan or marketing strategy. If the business is successful, the entrepreneur may want to consider expanding the business or exploring new opportunities.

On October 7th, the Kaiser's peace plea shared the front page with Easton's call for medical help. The local physicians were now unable to care for the increase in new cases, and the call for aid went to the State Health Commissioner. Extra forces had to be hired by cemeteries to dig graves, and a coffin shortage arose in Easton. The following notice appeared in October 7th's Easton Express.

"An Urgent Appeal to Every Woman in this Vicinity"

"The help of several hundred women - their personal help - must be had immediately. Women to help in families where there is influenza are needed by the Red Cross AT ONCE - needed as they have never been before.

Experience in nursing is not necessary. You are asked to help distracted families unable to secure assistance of any kind - to look after children - cook - give worn out father or mother a chance to snatch a little sleep - to do the many things that only a woman can do.

The concentrated action of several hundred women will stamp out our epidemic.

It will mean personal sacrifices and discomforts, but we believe this call - in the name of humanity - will be met by a prompt and willing response.

Call Mrs. E. P. Williams at once - phone Easton 19573. If you are unable to give a full day come for half a day or a few hours - only please report promptly.

If any one now employing nurses can release them it will greatly relieve the situation."

"Chairman Red Cross Nursing Committee"

In the same issue of the paper Dr. Royer, State Commissioner of Health, dispatched this message to Easton doctors. "Physicians of Easton take head: In Massachusetts pneumonia is less prevalent among influenza patients in canvas tents than in hospitals or private homes. Fewer nurses, doctors, and attendants sicken under canvas. Listen! Give influenza patients open window treatment, and where possible outdoor treatment." Advanced medical students from Philadelphia medical schools were sent to Easton to ease the doctor shortage.

Along with the fall of the Hindenburg Line and the decline of German resistance by October 9th, there seemed to be for the first time a parallel decline in the number of new influenza cases in Easton. Even now, however, the large number of cases necessitated the turning of the City Guard Armory into an emergency hospital. Area physicians were urged to report all new and old diagnosed cases of influenza so as to enable an accurate count. Florists of the area published their regrets that they could not supply ample flowers in view of the large number of funerals. The following day the epidemic situation in Easton was described to be at a standstill. Dr. Green stated that he thought the epidemic was now spreading west leaving Easton in its wake. Up to October 11th the record read 59 deaths from influenza in the Easton area. City Hall reported a new complication associated with the lessened epidemic activity. Aside from complaints about several saloons remaining open to sell drinks, Dr. Condren declared that there were many noticeably drunken men about town. This issue was sternly dealt with by Mayor Nevin who immediately closed all breweries. The new case rate continued to decline for the next few days, but death rates were still high. On October 15th the newspaper reported the largest number of deaths per day in the history of the city.

The total number had reached 111 since October first. Wholesale liquor stores were closed to tighten the quarantine, and beer was sold only by a doctor's prescription. October 18th saw 112 new cases of influenza reported. This was a decrease over the last week, but still too serious a threat to relax the quarantine. A kind retail liquor dealer in the city provided free whicky to all the worthy sick upon presentation of a prescription from their physician. The prescriptions were filled at City Hall under police supervision. Citizens were asked to please bring their own bottle and cork, and limit themselves to eight ounces.

On October 21, for the first time in 28 days, news of the influenza epidemic failed to make the first page of the Easton Express. Twenty-seven new cases were reported Wednesday, October 23, with one death. The total deaths now read 197. On October 24 no mention of the epidemic was made in the paper, and on the 25th the epidemic was felt to have left the city. The people of Easton, quickly tiring of the recent restrictions, pressed hard to remove their quarantine. The official records totalled 860 reported cases of influenza with 240 deaths during the month of October. Easton cemeteries recorded 450 burials during this time. On November 7 came the lifting of Easton's quarantine marking the end of the worst disaster ever to engulf the area. Ironically the quarantine was raised just in time to celebrate the end of another disaster, World War I. Peace came to the world November 11, 1918.

The epidemic left Easton on November eleventh, and soon life was back to normal among the inhabitants. Many will never forget the loss of their loved ones, but few realized that they had experienced the most catastrophic outbreak of infectious disease in modern times.¹ In the United

¹ Burnet, Frank M. Some biological implications of studies on influenza viruses. Johns Hopk. Hosp. Bull., 1951, 88, 137.

States the average mortality was 390 per 100,000 people, but variation was considerable from city to city. Variability was also a fact in the number of incidence and mortality peaks in different cities.¹ A so-called minor epidemic followed a year and one half to two years later, but in Chicago, Atlanta, and Kansas City this minor epidemic carried a higher mortality rate than the original 1918 episode.

¹ Burnet, Frank M. and Clark, Ellen. Op. cit., p. 75.

Chapter IV

Influenza Investigation

Medical observers now began to look back on the epidemic and found to their surprise that 50 per cent of the deaths were among the 20 to 40 year age group.¹ Also surprising was the finding that case incidence was highest among the 5 to 20 age range.² Various explanations were offered to explain these facts, but only postulations could be made until the development of more advanced investigative means.

The first and uniformly mild wave of the epidemic which appeared in the spring of 1918 was studied bacteriologically. Pfeiffer's bacillus was not found in a large enough number of cases to be considered the etiological cause.³ This was in contrast to findings reported during the second wave in the fall, during which Pfeiffer's bacillus was reported in 70 to 90 per cent of the cases.⁴ Shope stated that while some investigators were convinced by the 1918 bacteriological studies that Pfeiffer had been confirmed and that hemophilus influenzae actually was the cause of pandemic influenza, most people felt that some other explanation should be sought. Attempts were made at this time to demonstrate a viral etiology. Selter and Jaschke in 1918 claimed to have produced influenza with bacteria free filtrates of upper respiratory tract secretions from human influenza cases. Most of these experiments were largely negative, and were unrepro-

¹ Burnet, Frank M. and Clark, Ellen. Op. cit., p. 79.

² Smith, David T., Conant, Norman F., et al. Op. cit., p. 732.

³ Shope, Richard E. Old, intermediate, and contemporary contributions to our knowledge of pandemic influenza. Medicine (Baltimore), 1944, 23, 426.

⁴ McIntosh, J. The incidence of bacillus influenzae (Pfeiffer) in the present influenza epidemic. Lancet, 1918, 2, 697.

duceable by other workers here and abroad. Speculation was high nevertheless, and most thought it to be only a matter of time till the etiology of influenza was determined.

In 1930 Richard Shope described the presence of a filtrable agent in infectious material from cases of swine influenza that had definite pathogenic properties for swine when administered intranasally.¹ Subsequent study showed this to be a virus which was indistinguishable clinically or pathologically from the human form.² In 1933 Smith, Andrewes, and Laidlow successfully infected ferrets with bacteriologically sterile throat washings from influenza patients. The infected ferrets developed an influenza-like illness, and it was found that this could be transmitted to healthy ferrets. The causative agent possessed the characteristics of a filterable virus; thus at long last a laboratory animal was found in which the disease could be studied.³

The infected ferrets which recovered developed an immunity to subsequent infection with the same strain of virus, and human serum from influenza recovered patients neutralized this ferret influenza virus. Thomas Francis Jr. was able to reproduce these results using as his source human influenza cases in Puerto Rico.⁴ Shope's swine influenza created an influenza-like symptomatology in ferrets strikingly similar to the human type

¹ Shope, Richard E. Swine influenza. III. Filtration experiments and etiology. J. Exp. Med., 1931, 54, 384.

² Idem. Old, intermediate, and contemporary contributions to our knowledge of pandemic influenza. Medicine (Baltimore), 1944, 23, 432.

³ Smith, Wilson and Andrewes, C. H. A virus obtained from influenza patients. Lancet, 1933, 2, 66.

⁴ Francis, T. Jr. Transmission of influenza by a filtrable virus. Science, 1934, 80, 457-459.

suggesting a close antigenic relationship between the swine and human forms.¹

These advances fostered new interest in influenza research, and many workers began to add their contributions to the field. In 1933 Elford developed a gradocol membrane which made possible the first relatively accurate measurement of virus size.² In 1936 Magill and Francis found that various strains of influenza viruses were antigenically members of the same virus group. Serological types similar to the original strain isolated by Smith, Andrewes, and Laidlow were designated as influenza A.³ In 1940 Thomas Francis, Jr. described an immunologically distinct influenza virus, and reported it to be type B.⁴ In retrospect it was felt at this time by most workers that the mild wave of the 1918 epidemic was caused by the type A virus, and the more severe autumn wave had as its cause an immunologically related but not identical etiologic agent. There also appeared with the severe wave an unexplained pathological relationship with Pfeiffer's bacillus. Hirst, and independently McClelland and Hare in 1941, described virus hemagglutination as a method of group determination. F. M. Burnet in 1943 discovered that viruses could be cultivated in embryonated eggs.^{5,6,7}

¹ Smith, Wilson and Andrewes, C. H. Op. cit., 68.

² Burnet, Frank M. Op. cit., 119.

³ Horsfall, F.L. Jr., Lennette, E.H., Rickard, E.R., Andrewes, C.H., Smith, W. and Stuart-Harris, C.H. The nomenclature of influenza. Lancet, 1940, 2, 413-414.

⁴ Francis, T. Jr. A new type of virus from epidemic influenza. Science, 1940, 92, 408.

⁵ Hirst, George K. Direct isolation of human influenza virus in chick embryos. J. Immunol., 1942, 45, 295.

⁶ McClelland, Laurella and Hare, Ronald. The absorption of influenza virus by red cells and a new in vitro method of measuring antibodies for influenza virus. Canad. Publ. Hlth. J., 1941, 32, 530-538.

⁷ Burnet, F. M. Propagation of the virus of epidemic influenza on the developing egg. Med. J. Aust., 1935, 2, 687-689.

This made available large quantities of virus for experimental study and vaccine production. With the advent of penicillin in 1942, systemic antibiotic therapy was available to battle against secondary bacterial infection, long thought to be the prime factor accounting for the high mortality rates in major epidemics.

Chapter V

Influenza 1957

Many now seriously believed we were at last prepared for influenza. We were aware of the etiologic agent, we had means to provide immunity, and we could protect against secondary bacterial infection. All that now had to be done was to detect an incipient epidemic, and bring our forces into play to combat it. This exact situation arose in Asia in mid-1957. Our virologists, epidemiologists, and public health teams instantly began work to identify, classify, and prevent. It was found that the causative agent was a new antigenic strain of influenza virus A. The clinical course was generally mild, with chills, fever, aches, prostration, and coryza constituting the major symptomatology. The incidence in Asia was approximately 20 per cent of the population, mortality about 0.1 per cent, and most deaths occurred in the aged or debilitated. Thus the attack and the mortality rates were estimated to be much lower than the respective 50 and 3 per cent in 1918. The difference was accounted for by the fact that while the causative virus (Type A) was probably the same, the strain causing the earlier outbreak was far more virulent.¹

The medical profession felt at this time that vaccination constituted the most effective method of reducing the incidence and lessening the severity of the oncoming epidemic. Experiments indicated that such prophylaxis offered approximately 70 per cent protection. Because of the short incubation period of the disease (1-3 days) and the approximate

¹ Mattia, V. D. Jr. Asian influenza. Therapeia, 1957, 76, 2.

ten days required for immunization after vaccination, the program had to be carried out in advance of the epidemic. A multi-million dollar program was begun by six of the nation's leading drug manufacturers to produce monovalent and polyvalent vaccine containing inactivated virus derived from allantoic chick embryo fluid.

The vaccine process proved costly and the full manufacturing cycle took approximately 50 days. It was found that the vaccine had to be refrigerated during shipping as well as while in storage. The vaccine underwent chemical breakdown if stored at room temperature for more than five days and was as a result ineffective. Under refrigeration the vaccine remained effective up to 18 months. The success of the vaccine program to curtail the epidemic depended first upon the efficacy of the vaccine and second on the number of persons vaccinated by the time the epidemic struck. This 1957 program constituted the most comprehensive effort ever made to prevent an influenza epidemic. Shall we look at the results?

As was the case at the beginning of the influenza epidemic in Easton in 1918, again on October 1, 1957, the headlines of the Easton Express described American troop activity. The dashing exploits of Pershing's expeditionary forces were now replaced by the more degrading and disappointing news that federal troops were necessary to make it possible for negro students to attend Central High School in Little Rock, Arkansas. The paper also stated that during the week ending October first a sharp increase in school absences had been noted in the Easton area. Realizing the importance of early detection and remembering all too well 1918, county health officers ordered immediate tests to determine whether or

not the schools were dealing with Asian influenza. The case incidence according to medical observers seemed to be highest among children and young adults. Many schools in the area began to close as absentee numbers climbed, and Easton learned that it was again in the midst of an influenza epidemic. By October 12th, just two weeks after the first case reports, incidence rates began to fall, and some schools reopened their doors. The county health officials believed the area had experienced a mild form of influenza and felt that it had now passed, leaving no mortalities in its wake. One week later the incidence rate again rose, and Easton Hospital admitted nine cases of diagnosed influenza. The first death in the area attributed to influenza complications was among this group. By the end of October the hospital reported admitting approximately 35 cases during the one month period with symptoms characteristic of the epidemic disease. Of these, two deaths were attributed to Asian Influenza. These figures certainly differ from those reported by the County Medical Association at the end of the 1918 epidemic when there were 860 reported cases and 240 deaths in the Easton area. The lower incidence and mortality rates were explained by the state health officers as factors due to an etiological agent of lower virulence than the 1918 virus. It was also stated that increased immunity could be a factor in the relative mildness of the attack, but it must be mentioned that very few persons in the Easton area had received influenza vaccine due to a shortage of the vaccine prior to the attack. Easton was certainly more fortunate in 1957 in its relationship with influenza than it was in 1918, but still too many people suffered, and Easton has much to remember. The County Medical Society concentrating on the preventive aspect plans a major vaccination program at first notice of the next influenza wave in Easton.

During the fall of 1957 while in New Haven I personally witnessed and even became part of that city's influenza epidemic. The following is a description of the epidemic as seen as New Haven Hospital in respect to therapy and clinical course. The detail cited in the following paragraphs comes from a clinical study done by Dr. Robert G. Petersdorf at the Grace New Haven Community Hospital.

The expected Asian influenza epidemic appeared in New Haven in late September with its peak during the last two weeks in October. Throughout the approximately six-week period, 91 people were hospitalized with the diagnosis of Asian influenza. It is of interest that none of these had received any influenza vaccine. Among these 91 there were 11 deaths. A criterion for hospital admission had to be established to handle the sudden influx of patients into the emergency room at New Haven Hospital. Those with severe cough, positive findings on chest examination, or temperature elevation above 104° were admitted. The hospitalization of the 91 patients during the six-week period constituted a six-fold increase in pneumonia admissions over the same period in 1956. Within two weeks after this peak, pneumonia admissions returned to the pre-epidemic level.

Statistics showed the following: elderly males were more likely to develop pneumonia after influenza. Females were most susceptible to influenza during the child-bearing years. Negroes were more prone to the disease than whites. Laboratory studies revealed that 38 of these patients had bacterial pneumonia with D. pneumoniae being the most common offender; and 43 were free from bacterial invasion. Group sample studies made it almost certain that the Asian Influenza virus was a determining factor in the majority of these infections. It was also shown that pregnant patients and patients with heart or chronic lung disease appeared to be more suscep-

tible to post-influenza pulmonary infections. Antimicrobial therapy with antibiotics was instituted in the majority of cases with favorable results, but a number of the group with pneumonia in which no bacterial offender could be demonstrated did well without antibiotic therapy. This suggested a viral etiology.

Bloody sputum and leukopenia proved to be a poor prognostic sign. Of the 11 patients who died, 4 were elderly with chronic disease, but 7 were previously healthy adults. Antibiotics, adrenal cortical hormones, and supportive measures were ineffective in the fulminating course of their illness.

In retrospect, the epidemic in the New Haven area resulting in 11 fatalities differed greatly in incidence and mortality from the severe wave of the 1918 epidemic, but the fulminating pneumonia described in the New Haven study in 1957 is strikingly similar to that described by Chickering and Park in an army camp in 1918.¹

The conclusion drawn from the New Haven study is in agreement with Easton's plan that the most rational approach to the problem is early prophylaxis. It was learned that this is especially true and of prime importance to pregnant women, patients with heart disease, and people with chronic pulmonary insufficiency.

The epidemic left New Haven, traveled to Easton, and was over by the end of October. Some people breathed a sigh of relief, many regained their health, but a few of us realized that it would be only a matter of time until our cities would again be set upon by another seige of influenza.

¹ Chickering, N. T. and Park, J. H., Jr. Staphylococcus aureus pneumonia. J. Amer. Med. Ass., 1919, 76, 617-626.

Chapter VI

Conclusion

We have come a long way in medical research and clinical applications in the last fifty years. There remains in the forefront of our endeavors the ever elusive method or means to conquer the virus infection. Thirty-five years ago we learned about the presence of this entity, today we must find a weapon to combat it. This endeavour will occupy the life time work of many researchers. The answer, whether it encompasses chemotherapy, preventive medicine, or both will most certainly be used to solve the ever-present problem of the influenza epidemic. I personally hope that I will be able to offer more to my patients in Easton in the future than was available to those who suffered in 1918 and 1957.

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